

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCHING AUTHORITY

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/003711

International filing date (day/month/year)
07.04.2004

Priority date (day/month/year)
10.04.2003

International Patent Classification (IPC) or both national classification and IPC
A61N2/02, A61N2/00

Applicant
MARKOLL, Richard

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
 claims Nos. 1-6

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
 the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):
 the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for the whole application or for said claims Nos. 1-6
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- the written form has not been furnished
 does not comply with the standard
the computer readable form has not been furnished
 does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
 See separate sheet for further details

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	7-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	7-15
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	7-15
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III.

No examination will be carried out in respect of claims 1 to 6, because they have not been searched (see Art. 17(2)(a) or (3) PCT, Rule 66.1(e) PCT and the international search report).

Re Item V.

- 1 The following documents are referred to in this communication:
D1 : US 2002/042633 A1 (MARKOLL RICHARD) 11 April 2002 (2002-04-11)
D2 : US 2002/032148 A1 (ONO TAKASHI ET AL) 14 March 2002 (2002-03-14)
- 2 Document D1, which is considered to represent the most relevant state of the art for the subject-matter of independent claim 7, discloses (the references in parenthesis applying to this document) the treatment of patients with damaged cartilage by exposing them to electromagnetic signals generated by pulsating, pulse-modulated, unidirectional, direct current with frequency between 1 and 30 Hz and field strength from 1 to 20 G (see paragraph 21, 24 and claim 1).
The method disclosed in D1 is considered suitable for treating osteoporosis also (for the meaning of "suitable for", see the guidelines: C-III, 4.8 and C-IV, 7.6) due to the simultaneous administration of fibroblast growth factor (see also paragraph 12 of D1).

From this, the subject-matter of independent claim 7 differs in that botulinum toxin is used to prepare a pharmaceutical composition, which is simultaneously administered to the patients. The subject-matter of claim 7 is therefore novel (Article 33(2) PCT).

- 2.1 The problem to be solved by the present invention may be regarded as how to provide an alternative way of enhancing the treatment of osteoporotic patients with electromagnetic signals.
- 2.2 The solution to this problem proposed in claim 7 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

D2 is the only available prior art document referring (see paragraphs 5 and 11-16)

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AUTHORITY (SEPARATE SHEET)**

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to the experimental use of a botulinum toxin, namely the C3 enzyme, in the treatment of osteoporosis and states that this toxin cannot permeate cytoplasm and thus cannot be developed as a pharmaceutical agent. Therefore, document D2 leads the person skilled in the art away from the solution proposed in claim 7. The other A-documents cited in the international search report are considered less relevant.

Therefore, claim 7 involves an inventive step according to Art. 33(3) PCT.

- 2.3 Claims 8-15 are dependent on claim 7 and as such also meet the requirements of the PCT with respect to novelty and inventive step.